Dietary patterns associated with colon and rectal cancer: results from the Dietary Patterns and Cancer (DIETSCAN) Project^{1–3}

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ABSTRACT

Background: An analysis of dietary patterns or combinations of foods may provide insight regarding the influence of diet on the risk of colon and rectal cancer.

Objective: A primary aim of the Dietary Patterns and Cancer (DIETSCAN) Project was to develop and apply a common methodologic approach to study dietary patterns and cancer in 4 European cohorts: the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study (Finland–ATBC), the Netherlands Cohort Study (NLCS) on Diet and Cancer, the Swedish Mammography Cohort (SMC), and the Ormoni e Dieta nella Eziologia dei Tumori (Italy–ORDET). Three cohorts (ATBC, NLCS, and SMC) provided data on colon and rectal cancer for the present study.

Design: The cohorts were established between 1985 and 1992; follow-up data were obtained from national cancer registries. The participants completed validated semiquantitative food-frequency questionnaires at baseline.

Results: Exploratory factor analysis, conducted within each cohort, identified 3–5 stable dietary patterns. Two dietary patterns—Vegetables and Pork, Processed Meats, Potatoes (PPP)—were common across all cohorts. After adjustment for potential confounders, PPP was associated with an increased risk of colon cancer in the SMC women (quintile $4_{\rm multivariate}$ relative risk: 1.62; 95% CI: 1.12, 2.34; *P* for trend = 0.01). PPP was also associated with an increased risk of rectal cancer in the ATBC men (quintile $4_{\rm multivariate}$ relative risk: 2.21; 95% CI: 1.07, 4.57; *P* for trend = 0.05). Neither pattern was associated with the risk of colon or rectal cancer in the NLCS women and men.

Conclusion: Although certain dietary patterns may be consistent across European countries, associations between these dietary patterns and the risk of colon and rectal cancer are not conclusive. *Am J Clin Nutr* 2004;80:1003–11.

KEY WORDS Colorectal cancer, dietary pattern, Dietary Patterns and Cancer Project, DIETSCAN, factor analysis, principal components analysis

INTRODUCTION

Colorectal cancer is the second most common cancer, next to lung cancer for men and breast cancer for women, in Europe and North America (1). In Europe alone, 363 000 incident cases of colorectal cancer were reported in 2000. Approximately 6% of men and women are affected by age 75 y. In a recent report on Diet, Nutrition, and the Prevention of Chronic Disease (2), it is suggested that up to 80% of the differences in colorectal cancer rates between countries may be attributable to diet-related factors, particularly overweight or obesity and physical activity. The

expert panel also noted that "there is almost universal agreement that some aspects of the westernized diet are a major determinant of risk" and that "there is some evidence that risk is increased by high intakes of meat and fat, and that risk is decreased by high intakes of fruits and vegetables, dietary fiber, folate, and calcium, but none of these hypotheses has been firmly established."

Previous studies have focused on the association of those single nutrients or food groups with colorectal cancer outcomes. However, this reductionist approach does not take into account that foods and food constituents likely act synergistically (3). More recently, nutrition epidemiologists have used factor analysis to examine whether dietary patterns, or combinations of foods, are associated with colorectal cancer (4–7). Factor analysis disentangles complex dietary data into a small number of dietary characteristics (labeled as "patterns" according to their dominant foods) that are relatively independent from one another and that can be treated as risk factors in subsequent analyses of cancer risk. Results from such analyses (4, 5) have shown more consistent and stronger associations between certain dietary patterns and colorectal cancer than between individual nutrients or

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TABLE 1Characteristics of Dietary Patterns and Cancer (DIETSCAN) Project cohort studies with colon and rectal cancer cases¹

	-	-	NLCS	SMC
	ATBC men	NLCS men	women	women
Country	Finland	Netherlands	Netherlands	Sweden
Baseline years	1985-1988	1986	1986	1987-1990
Follow-up year	1999	1992	1992	2001
Baseline cohort size	29 133	$58\ 279^2$	62 573 ²	61 463
Age range (y)	50-69	55-69	55-69	40-74
Age (y)	57.2 ± 5.1^3	61.4 ± 4.2	61.4 ± 4.3	53.7 ± 9.7
BMI (kg/m^2)	26.3 ± 3.8	25.0 ± 2.6	25.1 ± 3.5	24.8 ± 4.4
Education: high school, vocational, or university training (%)	35.5	38.1	31.3	12.4
Smoking ⁴				
Cigarettes (no./d)	20.4 ± 8.8	14.5 ± 11.5	4.5 ± 7.5	_
Duration (y)	35.9 ± 8.4	28.9 ± 15.9	11.3 ± 15.8	_
Physical activity (%) ⁴				
Did not work	41.8	_	_	_
Active <30 min/d	_	18.35	24.7^{5}	_
Did mainly office work	14.0^{6}	_	_	_
Active 30–60 min/d	_	30.3^{5}	31.9^{5}	_
Walked a lot at work	18.5^{6}	_	_	_
Active 60–90 min/d	_	19.15	21.85	_
Walked and lifted a lot at work	16.6^{6}	_	_	_
Active >90 min/d	_	32.3^{5}	21.65	_
Did heavy physical labor at work	9.0^{6}	_	_	_

¹ ATBC, Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; NLCS, Netherlands Cohort Study on Diet and Cancer; SMC, Swedish Mammography Cohort.

foods and colorectal cancer. Such analysis of dietary patterns is promising but requires further investigation, particularly across cultures.

A primary aim of the Dietary Patterns and Cancer (DIETSCAN) project was to develop and apply a common methodologic approach to study dietary patterns and cancer in 4 European cohorts: the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study (ATBC; Finland), the Netherlands Cohort Study (NLCS) on Diet and Cancer, the Swedish Mammography Cohort (SMC), and the Ormoni e Dieta nella Eziologia dei Tumori (ORDET; Italy), and to determine whether the associations of those dietary patterns with cancer are consistent across cultures. Factor analysis was selected as the common method and was applied a posteriori to the dietary data collected in each cohort. This study reports findings from the factor analysis of dietary patterns and their association with colon and rectal cancer in 3 of the cohorts (ATBC, NLCS, and SMC) that provided colorectal cancer data.

SUBJECTS AND METHODS

Study population

Four European cohorts were selected for DIETSCAN because they were part of prospective cohort studies designed to investigate the effects of diet on the risk of various cancers and because they included a validated dietary assessment instrument to collect baseline dietary data of commonly consumed foods and beverages from the participants. Three of the DIETSCAN cohorts (ATBC, NLCS, and SMC) provided follow-up data on

colon and rectal cancer through record linkage of the cohorts with national cancer registries (**Table 1**). Colon cancers were defined as cancers occurring above the peritoneal delineation of the abdominal cavity [International Classification of Diseases, 9th revision (ICD-9) code 153], and rectal cancers were defined as cancers occurring below this delineation (ICD-9 code 154). A brief description of each cohort follows.

The ATBC Study was a randomized, double-blind, placebo-controlled chemoprevention trial of male smokers in southwestern Finland (8). Between 1985 and 1988, 29 133 men between the ages of 50 and 69 y who smoked \geq 5 cigarettes/d were randomly assigned to receive a daily dose of *all-rac-\alpha*-tocopherol (50 mg), β -carotene (20 mg), both, or a placebo. Before randomization, 27 111 men (93%) completed a 276-item food-frequency questionnaire (FFQ) that asked about consumption frequency and portion sizes of common foods and beverages in the previous year. Validity of the ATBC FFQ was determined by twelve 2-d food records collected from 190 men over 6 mo (9).

The NLCS on Diet and Cancer is a population-based prospective cohort study of 58 279 men and 62 573 women, selected from 204 Dutch municipalities with computerized population registries, who were between the ages of 55–69 y when the study began in 1986 (10). A case-cohort approach was used for data processing and analysis. In this design, a subcohort is randomly selected from the entire cohort, which provides a comparison group for each occurrence time, ie, those subjects in the subcohort who are still at risk for the disease under study at a given failure time serve as control subjects for the occurring failure,

² A subcohort of 3500 participants (1688 men, 1812 women) was followed biennially for vital status information.

 $^{^{3}\}bar{x} \pm SE$ (all such values).

⁴ Data not collected in the SMC.

⁵ Physical activity in the past year outside of work.

⁶ Physical activity in the past year while at work.

TABLE 2Characteristics of the food-frequency questionnaire (FFQ) and factor analysis-derived dietary patterns in the Dietary Patterns and Cancer (DIETSCAN) Project cohort studies¹

	ATBC men	NLCS men	NLCS women	SMC women	
Total no. of items	276	150	150		
FFQ reference period (mo)	12	12	12	6	
Frequency	Times per day, week, or month	7 categories (never to 6–7 times/wk)			
Quantification	Portion size picture booklet (3–5 per item)	Natural or household units (fixed weight per unit)	Natural or household units (fixed weight per unit)	Age-specific standard portion sizes	
No. of food groups used to determine factors	46	49	49	42	
No. of factors extracted	3	5	5	4	
Factor variance (%)					
Salad vegetables	9.7	5.6	6.3	6.8	
Pork, processed meats, potatoes Other factors (%)	5.4	4.2	4.3	5.3	
Alcohol	5.5	_	_	6.7	
Cooked vegetables	_	4.8	_	_	
Full-fat dairy products	_	_	4.4	_	
Brown- or white-bread substitute	_	4.1	4.3	_	
Bread, cheese, and cookies	_	_	_	4.6	
Sweet and savory snacks	_	4.3	3.9	_	
Mean total energy from FFQ (μJ/d)	6.73	9.04	7.07	5.56	

¹ FFQ, food-frequency questionnaire; ATBC, Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; NLCS, Netherlands Cohort Study; SMC, Swedish Mammography Cohort.

whether that failure occurs inside or outside the subcohort. A subcohort of 3500 participants (1688 men and 1812 women) was followed biennially for vital status information. At baseline, 1525 men and 1598 of the subcohort completed a mailed, self-administered questionnaire on dietary habits, including a 150-item FFQ that asked about usual intake of foods and beverages in the previous year. The NLCS FFQ was validated against 9-d dietary records from a subgroup of 109 participants (11).

The SMC comprises 61 463 women from Uppsala and Vastmanland counties in Sweden who were born between 1914 and 1948 and who were invited to participate in a population-based mammography screening program in 1987–1990 (12). The women completed a 67-item FFQ that asked about frequencies of intake of commonly consumed foods and beverages in the previous 6 mo. The SMC FFQ was validated against 4 sets of weighed 7-d food records from a subgroup of 129 women (6).

Human subjects

The ATBC Cancer Prevention Study was approved by the institutional review boards of the National Public Health Institute of Finland and the US. National Cancer Institute. The NLCS on Diet and Cancer was approved by the institutional review boards of the TNO Toxicology and Nutrition Institute (Zeist) and the University of Limburg (Maastricht) in the Netherlands. The SMC was approved by the Institutional Ethics Committee at Uppsala University and at Karolinska Institute, Stockholm.

Food grouping and assessment of dietary patterns

The validated semiquantitative FFQs used to collect dietary data at baseline differed by number of items, reference period, units of frequency and quantification of portion size, and overall level of detail (**Table 2**). To achieve the objectives of the

DIETSCAN Project, a common food grouping was developed (13). Food items from the FFQs were aggregated into 51 food groups that included foods common to all countries as well as specific foods included in each FFQ. These food groups were selected because of their role in the diet and possible relevance to cancer etiology.

To identify dietary patterns within each cohort, exploratory factor analysis using principal components analysis was conducted by using the grams per day of the total intake of the FFQ-derived food groups for each country. Food groups with >75% of 0, values representing nonusers, were dichotomized. Factors were rotated by orthogonal Varimax transformation. Eigenvalues >1 and the point at which the scree plot levels off, traditional criteria in factor analysis, were used to determine the number of factors to extract within each cohort (ie, 3 for ATBC, 5 for NLCS, and 4 for SMC).

Food groups with absolute factor loadings >0.35 were considered as contributing to a dietary pattern (**Appendix A**). Factor loadings represent correlation coefficients between food groups and dietary patterns. Food groups with positive loadings are positively associated with a dietary pattern; food groups with negative loadings are inversely associated with a dietary pattern. The proportion of variance explained by each factor was calculated by dividing the sum of the squares of the respective factor loadings by the number of variables (ie, food groups). The names of the dietary patterns within each cohort were determined according to the dominant foods (ie, foods with high loadings) in the respective patterns. The commonality of dietary patterns across cohorts was determined descriptively and named according to common dominant foods within the respective patterns.

Further detail regarding the food grouping and dietary pattern assessment, and related sensitivity analyses conducted in DIETSCAN, is provided by Balder et al (13).

Statistical analyses

Within the ATBC and SMC, Cox proportional hazards models were constructed to estimate hazard ratios and 95% CIs relating the common factors to the incidence of colorectal, colon, and rectal cancers. The NLCS used survival analysis with exponential distribution to estimate the SEs using the robust option to account for additional variance introduced by the case-cohort design. Before statistical analysis, factor scores were determined by summing the standardized intakes from each food group weighted by the factor loadings. Thus, within each cohort, each participant had a unique score for each factor. High scores represented a high intake of foods within the corresponding dietary pattern; low scores represented a low intake of those foods. Because factor scores represent standardized variables, each score had a mean of 0 and an SD of 1.

Within each cohort, the statistical models included all factor scores entered as linear (ie, one estimate per factor), as grouped (ie quartiles), or as grouped continuous with medians (ie, each group assigned the median value within each group) to test for linear trend. The models included all factor scores because dietary patterns are conditional on each other. The models were also adjusted for potential confounding variables determined by previous analyses of nutrients or food groups and incidence of colorectal cancer conducted within each cohort (14–16). In the ATBC, the models included age (<55, 55-59.9, 60-64.9, and \geq 65 y), treatment group (α -tocopherol, β -carotene, both, placebo), body mass index (BMI; in kg/m²) (<25, 25–27.4, and ≥27.5), level of education (primary, high school, vocational, and university), number of cigarettes smoked per day (<17, 17-20, and >20), number of years of smoking regularly (<33, 34-40, and >40 y), and occupational physical activity in the past year (not working, mainly office work, quite a lot of walking but no lifting or carrying, a lot of walking and lifting, and heavy physical work). In the NLCS, the models included age, BMI (<23, 23–25, 25–27, and >27), education (primary, junior high school, vocational, and high school/higher vocational/university), number of cigarettes smoked per day, number of years of smoking regularly, minutes per day of physical activity outside of the profession ($<30, 30-60, 60-90, and >90 \min/d$), and family history of colorectal cancer (yes, no). In the SMC, the models included age, BMI (quartiles), and education (less than high school, high school, and university). All models also included energy intake as a continuous variable. Because energy-contributing food groups tend to group together, pattern analysis was performed with the food group variables both unadjusted and adjusted for energy by using the residual method (17). The factor scores remained unadjusted in this analysis because energy adjustment of the food group variables yielded comparable factor solutions (13).

All reported *P* values are two-sided. PROC FACTOR and PROC PHREG in SAS version 8.2 (SAS Institute Inc, Cary, NC) were used to analyze the ATBC and SMC data. 'Streg, robust' in STATA version 6 (Stata Corporation, College Station, TX) was used to analyze the NLCS data.

RESULTS

With the use of a standardized approach, 3–5 stable dietary patterns were identified in cohort studies from Finland, the Netherlands, and Sweden (Table 2). Two dietary patterns, Vegetables (Veg) and Pork, Processed Meats, Potatoes (PPP) were observed in all 3 cohorts. The Veg pattern was characterized by intakes of vegetables and legumes, citrus fruit and berries, pasta and rice, poultry and fish, and oil and salad dressings (Appendix A) and was correlated with intakes of vitamins A, C, and E; folate; and polyunsaturated fatty acids. This pattern accounted for the most variance in dietary intake, ranging from 5.6% in the NLCS men to 9.7% in the ATBC men. The PPP pattern was characterized by intakes of pork, processed meats, potatoes, and coffee (Appendix A) and was correlated with intakes of energy, protein, carbohydrate, fat, saturated and monounsaturated fatty acids, cholesterol, B vitamins, and minerals. This pattern accounted for 4–5% of the variance in dietary intake across the cohorts. In general, both patterns were inversely correlated with age and positively but very weakly correlated with BMI, smoking, and physical activity in the cohorts. The Veg pattern was positively correlated with education, but only in the ATBC men.

In general, the Veg pattern was not associated with risk of colorectal, colon, or rectal cancer in the cohorts (**Table 3**). In the NLCS women, the Veg pattern was associated with a 14% reduced risk of colon cancer when included as a continuous variable in the age- and energy-adjusted model, but this pattern was not significant in the multivariate-adjusted model. In the ATBC men, the Veg pattern was associated with a 41–51% increased risk of colorectal cancer in the third quartile, but the test for trend was significant only in the age- and energy-adjusted model. Significant tests for trend in both models also suggested a positive association between the Veg pattern and rectal cancer in the ATBC men, but quartile risk estimates were not statistically significant.

The PPP pattern was associated with an increased risk of colorectal, colon, and rectal cancers in 2 of the cohorts (**Table 4**). In the SMC women, after adjustment for potential confounders, the PPP pattern was associated with an 18% increased risk of colorectal cancer when modeled as a continuous variable and a 37–61% increased risk in the fourth quartile of the categorical analyses with significant tests for trend. This pattern was associated with a similar increased risk of colon cancer in this cohort. In the ATBC men, the PPP pattern was associated with a 121% increased risk of rectal cancer (quartile 4) with a significant test for trend. The PPP pattern was not associated with a risk of colorectal, colon, or rectal cancers in the NLCS men and women.

DISCUSSION

The findings from DIETSCAN showed 2 consistent dietary patterns across the cohorts: one consisting mostly of vegetables (Veg) and one of pork, processed meats, and potatoes (PPP). A review of the literature on factor analysis of food consumption data showed these 2 patterns to be common across many different cultures, despite different methods of data collection and analysis and different numbers and types of foods consumed (18). In DIETSCAN, however, the associations of these 2 patterns with colorectal, colon, and rectal cancer were not as consistent. The Veg pattern was generally not associated with colorectal cancer in any cohort. The PPP pattern was associated with an increased

TABLE 3Relative risk (RR) of colorectal cancer by linear and quartile (Q) models of the Vegetable (Veg) pattern in the Dietary Patterns and Cancer (DIETSCAN) Project cohort studies ¹

		RR (95% CI)					
	1: PD2 (050) CD	Q1	02	02	C4	P for	
	Linear RR ² (95% CI)	(reference)	Q2	Q3	Q4	trend	
Colorectal cancer ATBC men	_	_	_	_	_	_	
Cases	322	68	64	101		_	
Person-years	286 967	69 360	70 433	72 421	74 753		
Age- and energy-adjusted model	1.10 (0.99, 1.23)	1.0	0.94 (0.66, 1.32)	1.51 (1.10, 2.05)	1.34 (0.97, 1.85)	0.02	
Multivariate model ³	1.07 (0.95, 1.20)	1.0	0.90 (0.64, 1.27)	1.41 (1.03, 1.93)	1.22 (0.87, 1.73)	0.09	
NLCS men		_					
Cases	660	162	168	167	163	_	
Person-years ⁴	10 496	2638	2604	2614	2640	_	
Age- and energy-adjusted model	1.06 (0.96, 1.17)	1.0	1.08 (0.83, 1.42)	1.14 (0.87, 1.49)	1.16 (0.88, 1.53)	0.27	
Multivariate model ⁵	1.03 (0.93, 1.15)	1.0	1.03 (0.78, 1.36)	1.04 (0.79, 1.38)	1.04 (0.78, 1.39)	0.41	
NLCS women				122			
Cases	512	134	131	132	115	_	
Person-years ⁴	11 328	2778 1.0	2810	2804	2936	0.42	
Age- and energy-adjusted model Multivariate model ⁵	0.90 (0.81, 1.01) 0.92 (0.81, 1.03)	1.0	1.02 (0.76, 1.36) 1.04 (0.77, 1.39)	1.05 (0.78, 1.42) 1.08 (0.79, 1.48)	0.87 (0.63, 1.20) 0.91 (0.65, 1.27)	0.42	
SMC women	0.92 (0.81, 1.03)	1.0	1.04 (0.77, 1.39)	1.06 (0.79, 1.46)	0.91 (0.03, 1.27)	0.78	
Cases	586	179	147	130	130		
Person-years	749 282	190 157	188 548	186 562	184 016		
Age- and energy-adjusted model	1.03 (0.93, 1.14)	1.0	0.85 (0.65, 1.12)	0.90 (0.68, 1.19)	0.97 (0.72, 1.30)	0.95	
Multivariate model ⁶	1.03 (0.93, 1.14)	1.0	0.91 (0.73, 1.13)	0.89 (0.70, 1.13)	0.99 (0.77, 1.27)	0.90	
Colon cancer		_				_	
ATBC men	_	_	_	_	_	_	
Cases	191	39	42	62	48	_	
Person-years	287 375	69 459	70 504	72 552	74 860		
Age- and energy-adjusted model	1.06 (0.92, 1.23)	1.0	1.05 (0.68, 1.63)	1.57 (1.05, 2.36)	1.22 (0.79, 1.88)	0.24	
Multivariate model ³	1.02 (0.87, 1.19)	1.0	0.99 (0.64, 1.54)	1.43 (0.95, 2.16)	1.05 (0.66, 1.67)	0.66	
NLCS men						_	
Cases	400	100	105	103	92	_	
Person-years ⁴	10 509	2638	2610	2615	2645	0.52	
Age- and energy-adjusted model Multivariate model ⁵	1.07 (0.95, 1.21) 1.02 (0.89, 1.16)	1.0 1.0	1.11 (0.80, 1.53) 1.04 (0.75, 1.46)	1.17 (0.85, 1.60) 1.03 (0.74, 1.43)	1.11 (0.80, 1.55) 0.93 (0.65, 1.32)	0.52 0.93	
NLCS women	1.02 (0.89, 1.10)	1.0	1.04 (0.73, 1.40)	1.03 (0.74, 1.43)	0.93 (0.03, 1.32)	0.93	
Cases	360	105	92	89	74		
Person-years ⁴	11 334	2778	2810	2810	2936		
Age- and energy-adjusted model	0.86 (0.75, 0.98)	1.0	0.92 (0.66, 1.27)	0.92 (0.66, 1.30)	0.74 (0.51, 1.07)	0.12	
Multivariate model ⁵	0.87 (0.76, 1.01)	1.0	0.94 (0.68, 1.31)	0.96 (0.67, 1.37)	0.78 (0.54, 1.15)	0.29	
SMC women			, , , ,	, , , ,			
Cases	396	122	94	91	89		
Person-years	749 964	190 356	188 763	186 681	184 165		
Age- and energy-adjusted model	1.03 (0.91,1.16)	1.0	0.85 (0.65, 1.12)	0.90 (0.68, 1.19)	0.97 (0.72, 1.30)	0.89	
Multivariate model ⁶	1.03 (0.91,1.16)	1.0	0.85 (0.65, 1.12)	0.90 (0.68, 1.19)	0.96 (0.71, 1.30)	0.87	
Rectal cancer							
ATBC men	122	20	22	40	41		
Cases	133 287 486	29 69 475	23 70 515	40 72 597	41 74 899		
Person-years Age- and energy-adjusted model	1.15 (0.98,1.36)	1.0	0.81 (0.47, 1.40)	1.44 (0.89, 2.33)	1.51 (0.93, 2.46)	0.02	
Multivariate model ³	1.14 (0.95,1.36)	1.0	0.80 (0.46, 1.38)	1.40 (0.86, 2.30)		0.02	
NLCS men	1.14 (0.55,1.50)	1.0	0.00 (0.40, 1.30)	1.40 (0.60, 2.50)	1.40 (0.00, 2.47)	0.04	
Cases	260	62	63	64	71		
Person-years ⁴	10 525	2645	2612	2621	2647		
Age- and energy-adjusted model	1.04 (0.91, 1.19)	1.0	1.04 (0.70, 1.54)	1.09 (0.74, 1.62)	1.23 (0.84, 1.81)	0.26	
Multivariate model ⁵	1.05 (0.91, 1.21)	1.0	0.99 (0.66, 1.49)	1.08 (0.73, 1.61)	1.23 (0.83, 1.83)	0.16	
NLCS women			. , ,	, , ,			
Cases	152	29	39	43	41		
Person-years ⁴	11 355	2782	2815	2812	2946		
Age- and energy-adjusted model	1.01 (0.85, 1.20)	1.0	1.39 (0.84, 2.30)	1.53 (0.91, 2.56)	1.34 (0.76, 2.36)	0.37	
Multivariate model ⁵	1.01 (0.85, 1.21)	1.0	1.40 (0.83, 2.34)	1.51 (0.89, 2.58)	1.33 (0.76, 2.35)	0.24	
SMC women	4 4			•			
Cases	193	57	56	39	41		
Person-years	750 318	190 477	188 768	186 804	184 270	c ==	
Age- and energy-adjusted model	1.07 (0.88, 1.31)	1.0	1.18 (0.80, 1.72)	0.93 (0.60, 1.43)	1.15 (0.72, 1.83)	0.75	
Multivariate model ⁶	1.06 (0.87, 1.29)	1.0	1.17 (0.80, 1.71)	0.92 (0.60, 1.41)	1.12 (0.70, 1.79)	0.84	

¹ ATBC, Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; NLCS, Netherlands Cohort Study; SMC, Swedish Mammography Cohort.

² The factor scores in the linear models are standardized variables with a mean of 0 and an SD of 1.

³ Includes age, ATBC treatment group, BMI, education, smoking (number of cigarettes/d, years smoked), occupational activity, and energy intake.

⁴ For the subcohort only.

⁵ Includes age, BMI, education, smoking (number of cigarettes/d, years smoked), physical activity, family history of colorectal cancer, and energy intake.

⁶ Includes age, BMI, education, and energy intake.

TABLE 4
Relative risk (RR) of colorectal cancer by linear and quartile (Q) models of the Pork, Processed Meats, Potatoes (PPP) pattern in the Dietary Patterns and Cancer (DIETSCAN) Project cohort studies ¹

	RR (95% CI)					
	Linear RR ² (95% CI)	Q1 (reference)	02	02	04	P fo
	Lillear KK (95% CI)	(reference)	Q2	Q3	Q4	treno
Colorectal cancer						
ATBC men Cases	322	70	84	91	71	
Person-years	286 967	69 852	71 593	72 836	72 685	
Age- and energy-adjusted model	0.94 (0.77, 1.14)	1.0	1.30 (0.93, 1.82)	1.48 (1.03, 2.13)	1.36 (0.85, 2.18)	0.21
Multivariate model ³	0.97 (0.79, 1.14)	1.0	1.34 (0.96, 1.88)	1.59 (1.10, 2.29)	1.49 (0.93, 2.39)	0.21
NLCS men	0.57 (0.75, 1.10)	1.0	1.54 (0.70, 1.00)	1.57 (1.10, 2.27)	1.47 (0.73, 2.37)	0.10
Cases	660	172	169	177	142	_
Person-years ⁴	10 496	2551	2579	2573	2793	_
Age- and energy-adjusted model	0.99 (0.88, 1.12)	1.0	1.02 (0.78, 1.34)	1.13 (0.85, 1.50)	0.90 (0.65, 1.24)	0.67
Multivariate model ⁵	0.98 (0.86, 1.11)	1.0	0.99 (0.75, 1.30)	1.11 (0.83, 1.49)	0.90 (0.65, 1.26)	0.75
NLCS women	,		(, , , , , , , , , , , , , , , , , , ,	(,,	, , , ,	
Cases	512	122	131	149	110	_
Person-years ⁴	11 328	2869	2803	2685	2972	
Age- and energy-adjusted model	0.98 (0.89, 1.09)	1.0	1.08 (0.81, 1.45)	1.35 (1.02, 1.80)	0.92 (0.68, 1.25)	0.98
Multivariate model ⁵	0.96 (0.86, 1.08)	1.0	1.08 (0.80, 1.46)	1.31 (0.97, 1.77)	0.89 (0.64, 1.23)	0.88
SMC women						
Cases	586	193	150	143	100	_
Person-years	749 282	188 421	182 974	189 625	188 263	
Age- and energy-adjusted model	1.18 (1.02, 1.37)	1.0	1.05 (0.79, 1.38)	1.21 (0.90, 1.64)	1.61 (1.11, 2.33)	0.0
Multivariate model ⁶	1.18 (1.02, 1.37)	1.0	1.04 (0.83, 1.29)	1.26 (0.99, 1.61)	1.37 (1.00, 1.89)	0.0
Colon cancer						
ATBC men	101	12	Ē1	5.0	4.1	
Cases	191	43	51	56 72 931	41 72 808	
Person-years	287 375	69 943 1.0	71 693 1.21 (0.79, 1.86)		0.99 (0.54, 1.85)	0.9
Age- and energy-adjusted model Multivariate model ³	0.81 (0.63, 1.05) 0.85 (0.66, 1.10)	1.0	1.26 (0.82, 1.94)	1.34 (0.84, 2.14) 1.47 (0.92, 2.35)	1.12 (0.60, 2.09)	0.9.
NLCS men	0.83 (0.00, 1.10)	1.0	1.20 (0.62, 1.94)	1.47 (0.92, 2.33)	1.12 (0.00, 2.09)	0.0
Cases	400	112	98	105	85	
Person-years ⁴	10 509	2 551	2 579	2 579	2 800	
Age- and energy-adjusted model	0.97 (0.84, 1.13)	1.0	0.93 (0.68, 1.29)	1.09 (0.78, 1.52)	0.91 (0.62, 1.33)	0.8
Multivariate model ⁵	0.98 (0.84, 1.15)	1.0	0.9 (0.65, 1.27)	1.1 (0.77, 1.57)	0.96 (0.65, 1.44)	0.89
NLCS women	., ., ., ., .,		*** (****, **=*)	(,,	(,)	
Cases	360	81	98	105	76	_
Person-years ⁴	11 334	2 869	2 803	2 685	2 978	
Age- and energy-adjusted model	0.99 (0.88, 1.11)	1.0	1.22 (0.87, 1.70)	1.43 (1.03, 1.99)	0.98 (0.68, 1.39)	0.8
Multivariate model ⁵	0.96 (0.84, 1.09)	1.0	1.22 (0.86, 1.72)	1.37 (0.97, 1.95)	0.92 (0.63, 1.35)	0.8
SMC women						
Cases	396	118.0	98	93	87	_
Person-years	749 964	188 729	183 164	189 780	188 292	_
Age- and energy-adjusted model	1.25 (1.05, 1.49)	1.0	1.05 (0.79, 1.38)	1.21 (0.90, 1.64)	1.61 (1.11, 2.33)	0.0
Multivariate model ⁶	1.25 (1.05, 1.49)	1.0	1.05 (0.80, 1.39)	1.22 (0.90, 1.65)	1.62 (1.12, 2.34)	0.0
Rectal cancer						
ATBC men	122	27	2.4	25	27	
Cases	133	27 69 962	34 71 747	35	37	_
Person-years	287 486 1.14 (0.84, 1.54)	1.0		72 973	72 804 2.11 (1.03, 4.33)	0.0
Age- and energy-adjusted model			1.47 (0.86, 2.49)	1.68 (0.94, 3.00)		
Multivariate model' NLCS men	1.15 (0.85, 1.57)	1.0	1.50 (0.88, 2.55)	1.75 (0.98, 3.15)	2.21 (1.07, 4.57)	0.0
Cases	260	60	71	72	57	_
Person-years ⁴	10 525	2 557	2 588	2 585	2 795	
Age- and energy-adjusted model	1.02 (0.86, 1.20)	1.0	1.18 (0.80, 1.74)	1.22 (0.82, 1.83)	0.89 (0.56, 1.42)	0.6
Multivariate model ⁵	0.98 (0.82, 1.17)	1.0	1.15 (0.78, 1.70)	1.14 (0.75, 1.73)	0.83 (0.51, 1.34)	0.4
NLCS women	(, 1-1)		(, 1)	(, 1)	(,)	0.1
Cases	152	41	33	44	34	
Person-years ⁴	11 355	2 880	2 808	2 690	2 977	_
Age- and energy-adjusted model	0.98 (0.83, 1.15)	1.0	0.81 (0.49, 1.32)	1.21 (0.76, 1.92)	0.82 (0.50, 1.35)	0.7
Multivariate model ⁵	0.97 (0.80, 1.16)	1.0	0.80 (0.47, 1.34)	1.19 (0.74, 1.93)	0.82 (0.48, 1.39)	0.9
SMC women	, , , ,			, , ,		
Cases	193	76	52	52	13	_
Person-years	750 318	188 765	183 225	189 862	188 466	
Age- and energy-adjusted model	0.95 (0.71, 1.26)	1.0	0.97 (0.66, 1.41)	1.26 (0.83, 1.90)	0.54 (0.26, 1.12)	0.52
Multivariate model ⁶	0.95 (0.72, 1.27)	1.0	0.98 (0.67, 1.44)	1.28 (0.85, 1.93)	0.56 (0.27, 1.17)	0.6

¹ ATBC, Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; NLCS, Netherlands Cohort Study; SMC, Swedish Mammography Cohort.

² The factor scores in the linear models are standardized variables with a mean of 0 and an SD of 1.

³ Includes age, ATBC treatment group, BMI, education, smoking (number of cigarettes/d, years smoked), occupational activity, and energy intake.

⁴ For the subcohort only.

⁵ Includes age, BMI, education, smoking (number of cigarettes/d, years smoked), physical activity, family history of colorectal cancer, and energy intake.

⁶ Includes age, BMI, education, and energy intake.

risk of colorectal and colon cancer in the SMC women and with an increased risk of rectal cancer in the ATBC men.

Our findings regarding the PPP pattern generally agree with those of other diet and cancer studies that used factor analysis to characterize dietary patterns. Slattery et al (5) identified a Western pattern of red meats, processed meats, fast food, refined grains, and sugar-containing foods that was associated with an increased risk of colon cancer in both men [odds ratio (OR): 1.80; 95% CI: 1.28, 2.53: *P* for trend < 0.01] and women (OR: 1.49; 95% CI: 1.05, 2.12; P for trend = 0.02) in a multicenter US population-based case-control study. Fung et al (7) identified a similar Western pattern of red and processed meats, French fries, refined grains, and sweets and desserts that was suggestive of an increased risk of colorectal cancer [relative risk (RR): 1.46; 95% CI: 0.97, 2.19; P for trend = 0.02] in a large prospective study of nurses in the United States. Randall et al (4) identified a Traditional pattern of meats, common vegetables (eg, green beans and corn), and baked goods that was associated with an increased risk of colon cancer (OR: 1.28; 95% CI: 1.04, 1.57) in a study of 205 men and 1475 neighborhood controls in Western New York. In a previous analysis of SMC data that used only 24 food groups, compared with 42 food groups in DIETSCAN, Terry et al (6) identified a Western dietary pattern of processed and red meats, soda and sweets, refined breads and potatoes, and high-fat dairy products, but this pattern was not associated with an increased risk of colorectal cancer.

The previous studies also identified a pattern comprising vegetables and other "healthful" foods that was generally associated with a reduced risk of colorectal cancer. In the US populationbased case-control study conducted by Slattery et al (5), a Prudent pattern of vegetables and fruits was associated with a reduced risk of colon cancer in both men (OR: 0.66; 95% CI: 0.50, 0.86; P for trend = 0.02) and women (OR: 0.73; 95% CI: 0.55, 0.97; P for trend = 0.02). Fung et al (7) also identified a Prudent pattern of vegetables, fruits, legumes, fish, poultry, and whole grains that was inversely but not significantly associated with colon cancer (RR: 0.71; 95% CI: 0.50, 1.00; P for trend = 0.31) in US nurses. In the case-control study in Western New York, Randall et al (4) showed a pattern of Salad vegetables to be associated with a reduced risk of colon cancer in women (OR: 0.73; 95% CI: 0.60, 089) and to be nearly significant in men (OR: 0.84; 95% CI: 0.69, 1.02).

We hypothesized that the Veg pattern would be associated with a reduced risk of colon and rectal cancers, but there was only slight evidence of this in the NLCS women. Our findings may differ from those of the previous US studies because of the types of foods included in the Veg factor. Our "healthful" pattern (Veg) included salad vegetables and fruit but also included high-fat foods such as salad dressings and high-starch foods such as pasta and rice. It is also possible that the dietary patterns common to different European cohorts may reflect differences across countries in the consumption of those foods (Appendix A) and may differ from the amounts typically consumed in the United States.

In addition, findings from analyses of dietary patterns may not always agree with findings from single foods or nutrients with cancer within the same study population. For example, the results from previous analyses of individual nutrients and foods with colorectal cancer in the ATBC and SMC tend to differ from our findings from the DIETSCAN analyses. In the ATBC men, calcium, milk protein, and milk products were inversely associated with risk of colorectal cancer, but meat, vegetables, and fruit

were not associated (14). In contrast, our results indicated that the PPP pattern, which reflects a high meat intake and is more strongly associated with dietary calcium and milk products than are the other patterns, was associated with increased risk. One possible explanation for this difference was that the factor analysis did not produce an independent dietary factor representing milk products as the dominant foods in the ATBC men. In the SMC women, total vegetable and fruit intake was associated with a reduced risk of colorectal cancer (16), whereas our results and those of a previous factor analysis (6) did not show a protective effect of the Veg pattern. However, the Veg pattern included foods other than vegetables and fruit, reflecting more complex dietary behavior rather than individual foods. Given that it is unlikely that any single food causes cancer, the strength of factor analysis of complex dietary data is the ability to assess many combinations of foods rather than single food groups that are rarely eaten alone. Thus, results from such analyses may lead to new hypotheses for dietary factors and cancer.

Limitations of factor analysis include the following. Although this statistical method is data driven and may be considered objective because it is conducted a posteriori, the analytic process is filled with subjective decisions such as the number and type of food groups determined from an FFQ, estimation of grams per day versus frequencies of food groups, transformation of food groups before principal components analysis, the criteria used to determine how many factors to extract (eg, Eigenvalue cutoff, interpretation of the scree plot), the rotation used, the interpretation of the resulting dietary patterns, and the use of factor or sum scores in the analyses of cancer outcomes (19). To address some of these limitations, we minimized the differences in the FFQ data and the detail and number of input variables in our factor analysis by aggregating the food items into a predefined, common food grouping. We also conducted sensitivity analyses with dichotomization of extremely skewed variables, the number of factors extracted, and the energy adjustment of the food group variables with the residual method. The results from these sensitivity analyses showed the Veg and PPP patterns to be robust and the associations with colorectal cancer to be consistent in each cohort (13).

It is possible that our findings are due, in part, to measurement error in the dietary data and to differences among the cohorts. Recent research shows the measurement error of FFQs to be larger than previously thought, which likely reduces the magnitude of risk estimates for the association of dietary patterns with cancer (20, 21). Also, although the simple age- and energyadjusted models were uniform across the cohorts, the multivariate models reflect differences in sociodemographic and behavioral data available from each cohort. For example, the SMC did not collect data on family history of colorectal cancer, physical activity, or smoking. The lack of data on other risk factors of colorectal cancer (eg, aspirin use) limits the analysis of interactions between the dietary patterns and these potential confounders across the cohorts. In addition, the participants in the ATBC (ie, male smokers) and the SMC (ie, women who responded to a mammography screening) may not be representative of the general population in their respective countries. Although DIETSCAN is not exempt from these limitations, it is important to emphasize that each study has the merits of being a large prospective cohort with validated semiquantitative FFQ, pathologically confirmed cases of incident cancers, and extensive follow-up data. Given that the dietary patterns were qualitatively

robust across the different cohorts, an analysis of the association of these patterns with other cancers (eg, breast and lung) may be more informative.

In conclusion, dietary patterns represent combinations of foods and may also represent biological interactions and nonnutrient substances that are difficult to assess. Although an analysis of dietary patterns has great potential to improve dietary guidance and public health and to create more successful dietary interventions, our opinion is that such an analysis complements, rather than replaces, findings from more traditional analyses of single nutrients or food groups with cancer. Results from DIETSCAN show 2 dietary patterns to be consistent across 3 European countries, but the association of these dietary patterns with the risk of colon and rectal cancer is not conclusive.

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RAG was the Principal Investigator of DIETSCAN and designed the study. RAG, PAvdB, PP, AMH, JV, and AW were the Principal Investigators of the DIETSCAN cohorts and participated in the acquisition and interpretation of data from their respective cohorts and in all DIETSCAN research activities. HFB, MJV, LBD, SM, BR, and VK conducted the statistical analyses of the DIETSCAN data. FT provided statistical consultation. LBD wrote the manuscript collaboratively with all coauthors. None of the authors had any financial or personal interest in the agencies that funded this study.

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APPENDIX A
Factor loads and intakes derived from food-frequency questionnaires for food groups that represent the common patterns in the Dietary Patterns and Cancer (DIETSCAN) Project cohort studies¹

	ATBC men		NI	NLCS men		NLCS women		SMC women	
Factors and representative food groups	Load	Intake ²	Load	Intake ²	Load	Intake ²	Load	Intake ²	
Vegetables		g/d		g/d		g/d		g/d	
Legumes	0.34	5 ± 5	0.11	40 ± 26	0.55	35 ± 23	-0.01	11 ± 15	
Cabbages	0.61	14 ± 16	0.13	40 ± 25	0.59	39 ± 24	0.43	10 ± 18	
Leaf vegetables, cooked	0.23	0.2 ± 1^{3}	0.01	22 ± 18	0.48	22 ± 16	0.25	8 ± 16	
Leaf vegetables, raw	0.69	1 ± 2	0.40	10 ± 10	0.52	10 ± 9	0.63	17 ± 16	
Allium vegetables	4	4	0.51	31 ± 27	0.59	31 ± 25	4	4	
Carrots	0.51	14 ± 17	0.20	12 ± 14	0.50	13 ± 16	0.59	24 ± 26	
Tomatoes	0.67	24 ± 22	0.45	20 ± 21	0.45	24 ± 21	0.56	27 ± 26	
Mushrooms	0.31	3 ± 5	0.52	3 ± 4	0.39	4 ± 4	4	4	
Citrus fruit	0.41	59 ± 79	0.21	51 ± 61	0.18	73 ± 67	0.50	52 ± 57	
Apples and pears	0.27	30 ± 42	-0.01	67 ± 75	0.17	84 ± 82	0.51	67 ± 67	
Berries, all types	0.35	36 ± 36	0.14	7 ± 8	0.12	8 ± 9	4	4	
Rice	0.48	6 ± 7	0.43	12 ± 30	0.35	9 ± 20	0.18	2 ± 6	
Pasta	0.33	8 ± 12	0.53	7 ± 9	0.36	5 ± 8	0.02	15 ± 14	
Poultry, fresh	0.41	12 ± 15	0.30	13 ± 15	0.24	14 ± 16	0.22	7 ± 7	
Fish, including shellfish and crustaceans	0.26	39 ± 30	0.29	14 ± 16	0.33	12 ± 14	0.41	25 ± 17	
Oil	0.27	2 ± 3	0.58	2 ± 3	0.41	2 ± 3	4	4	
Dressings and other similar sauces	0.77	2 ± 3	0.07	4 ± 6	0.16	5 ± 6	4	4	
Wine and fortified wine	-0.01	30 ± 42	0.40	33 ± 70	0.15	35 ± 64	0.09	15 ± 21	
Pork, Processed Meats, Potatoes									
Pork, fresh	0.54	41 ± 21	0.48	45 ± 33	0.43	39 ± 31	0.57	20 ± 17	
Processed meats	0.42	75 ± 59	0.53	22 ± 19	0.50	15 ± 14	0.42	25 ± 17	
Potatoes and potato products	0.55	180 ± 79	0.38	150 ± 85	0.29	101 ± 60	0.15	95 ± 52	
Coffee	0.23	607 ± 351	0.50	574 ± 292	0.44	495 ± 242	0.08	427 ± 202	
Beef and veal	0.32	26 ± 21	-0.11	44 ± 29	-0.07	37 ± 26	0.60	26 ± 18	
Pasta	0.10	8 ± 12	0.20	7 ± 9	-0.05	5 ± 8	0.55	15 ± 14	
Rice	0.04	6 ± 7	-0.18	12 ± 30	-0.31	9 ± 20	0.47	2 ± 6	
Eggs	0.46	53 ± 38	0.19	17 ± 13	0.14	15 ± 10	0.18	7 ± 8	
Poultry	0.08	12 ± 15	-0.01	13 ± 15	0.02	14 ± 16	0.40	7 ± 7	
Liver	0.19	3 ± 4	0.10	2 ± 5	0.28	2 ± 4	0.40	4 ± 5	
Butter	0.46	39 ± 30	-0.30	9 ± 16	-0.45	7 ± 12	0.02	4 ± 8	
Low-fat margarine	_4	4	0.46	8 ± 16^{3}	0.50	7 ± 13	_4	_4	
Wine	0.49	30 ± 42	-0.09	33 ± 70	-0.09	35 ± 64	0.00	15 ± 21	
Spirits	0.49	31 ± 43	-0.03	25 ± 40	0.07	4 ± 16^3	0.01	1 ± 2	

 $^{^{}I}$ Food groups that are listed for each pattern have factor loads ≥ 0.35 in at least one of the DIETSCAN cohorts.

 $^{^2\}bar{r} + SD$

³ Food groups with >75% of participants reporting no intake.

⁴ Food groups missing from the food-frequency questionnaire and thus not entered into the principal components analysis.